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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/088,072 | 07/03/2002 | Denis-Claude Roy | 220303US0 XPCT | 7574 |

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| EXAMINER | |
|---|---|
| HANLEY, SUSAN MARIE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1651 | |

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/088,072 | ROY ET AL. | |
| | Examiner | Art Unit | |
| | Susan Hanley | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *2-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040126*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

***Election/Restrictions***

Applicant's election with traverse of Group I, claim 1,. received on January 26, 2004 is acknowledged. The traversal is on the ground(s) that there is no evidence that proves that Groups I-VI are independent and distinct. Applicant also argues that the office has implicated that the compounds of Group I are not novel or unobvious in view of US 4,686,521 without an examination of the claims on the merits. Applicant further sates that the holding of lack of unity is not correct because all of the claims require the compounds of claim 1. Applicant further argues that the Office has not applied the same standard of unity of invention as the International Preliminary Examining Authority, wherein the IPEA made no holding of lack of unity. Applicant cites PCT Article 27(l) in support of this argument. Lastly, Applicant states that a search of all of the claims would not impose a serious burden on the examiner.. This is not found persuasive because the claims were properly restricted under Rule 13 of the PCT treaty, which states:

> Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

In the instant case, the unity of invention is destroyed because the compounds of claim 1 are disclosed by US 4,686,521. Therefore, the claimed inventions lack a special technical feature that define a contribution over the prior art since they are disclosed by the prior art. Since a holding of lack of unity was properly made, the inventions are therefore independent and distinct by the standards of the PCT Treaty. Also, the lack of unity holding shows that there is a serious burden to the examiner since the inventions are not connected by a special technical feature. Further, the PCT treaty does not require that the IPEA and the national stage examiner take the same position with regard to lack of unity. Applicants reliance on the PCT Article 27(l) is not relevant to the argument because PCT Article 27(l) deals with requirements regarding the form or content of the international application. Further, Article 27 (5) states that the PCT treaty regulations should not limit the freedom of the Contracting State to determine patentability. Regarding Applicants statement that the Office has implicated [sic] that the compounds of claim 1 are

neither novel nor unobvious is not well taken. Applying a citation for a finding of lack of unity is proper according to the requirements of 35 U.S.C. 121 and 372. Hence, no improper examination has been made .

The requirement is still deemed proper and is therefore made FINAL.

Claims 2-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claim 1 is presented for examination.

This requirement is still deemed proper and is therefor made **FINAL**.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,556,992. Although the conflicting claims are not identical, they are not patentably distinct from each other because the rhodamine derivatives disclosed by Gaboury et al. are the chloride salts of the instantly claimed five compounds of claim 1 (see col. 4, lines 64-67 through col. 5, lines 1-5). Claim 1 of the instant application names the bromide salts and "photoactivable derivatives thereof". The specification defines a photoactivable derivative as "substituted rhodamine 110 compounds and their salts". The compounds disclosed by Gabroury et al. are consistent with the given definition because the chloride salt is a specie that belongs to the genus of salts, as defined by the instant specification.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to five compounds. Each compound is named in two ways. First, the compound is claimed as a derivative of a rhodamine, wherein the rhodamine referred to by an abbreviation. The compound is then named by its chemical name. This is confusing because the derivatized, abbreviated name is not consistent with the chemical name. Specifically, the salts are different. For instance, 4,5-dibromorhodamine 123 refers to the 4,5-dibromo derivative of rhodamine 123. According to the CAS Registry file, rhodamine 123 is a chloride salt. However, the chemical name is drawn to a bromide salt. This inconsistency is confusing and it is unclear which compound Applicant intends to claim. The inconsistency follows for the compounds named as derivatives of rhodamine 110 and Rhodamine B. Rhodamine 110 and Rhodamine B are also chloride salts whereas the chemical nomenclature for the claimed compound is drawn to the bromide salt.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Gaboury et al.(US 5,556,992) or Gaboury et al. (US 5,773,460).

Gaboury et al. (US 5,556,992 or US 5,773,460) disclose rhodamine derivatives for photodynamic therapy of cancer. The photodynamic compounds are the chloride salts of the instantly claimed five compounds of claim 1 (for US 5,556,992, see col. 4, lines 64-67 through col. 5, lines 1-5; for US 5,773,460, see the abstract). Instant claim 1 names the bromide salts and "photoactivable derivatives thereof". The specification defines a photoactivable derivative as "substituted rhodamine 110 compounds and their salts". The compounds disclosed by Gabroury et al. are consistent with the given definition because the chloride salt is a specie that belongs to the genus of salts, as defined by the specification. Hence, Gabroury et al. (US 5,556,992 or US 5,773,460) anticipate claim 1.

Claim 1 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Pal et al. (1996).

Pal et al. disclose photoactivable agents comprising rhodamine derivatives. Pal et al. specifically teaches the chloride salt of two compounds in instantly claimed 1. They are the 4,5 dibromo rhodamine methyl ester and n-butyl ester hydrochloride salts (see the scheme on p. 163, dye 2 and dye 3, respectively). ". The compounds disclosed by Pal et al. are consistent with the given definition because the chloride salt is a specie that belongs to the genus of salts, as defined by the specification. Hence, Pal et al. anticipate claim 1.

Claim 1 is rejected under 35 U.S.C. 102(a) as being clearly anticipated by Villeneuve (published and available to the public on the Internet July 19, 1999).

Villeneuve discloses TH9402, 4,5-dibromorhodamine 123 for use in photodynamic therapy (abstract). As previously discussed, rhodamine 123 refers to a chloride salt. Hence, TH9402 is a chloride salt. The compound disclosed by Villenueve is consistent with the given definition because the chloride salt is a specie that belongs to the genus of salts, as defined by the specification. Hence, Villenueve anticipates claim 1.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gaboury et al. (US 5,556,992), Gaboury et al. (US 5,773,460), Pal (1996), or Villeneuve (published and available to the public on the Internet July 19, 1999) in view of Lucas et al. (US 5,871,946).

The disclosures of Gaboury et al. (US 5,556,992), Gaboury et al. (US 5,773,460), Pal (1996), and Villeneuve (1999) are set forth *vide supra*. Briefly, the four documents disclose the hydrochloride salt of some or all of the rhodamine derivatives of claim 1 for treating cancer by destroying cancer cells by for photodynamic therapy.

None of the references teach using the hydrobromide salts of the disclosed compounds for photodynamic therapy to treat cancer by destroying cancer cells.

Lucas et al. teach an assay compound or a salt thereof for assaying the activity of an enzyme inside a metabolically active whole cell. The assay compound comprises an indicator group that is preferably rhodamine 110. The assay compound is reacted with an acid or base to make a physiologically acceptable salt. Lucas et al. teach that HBr salts of rhodamines are more toxic to cells that their HCl counterparts. The exchange of HCl for HBr in rhodamine salts destroys cell viability. The toxicity of various salts of rhodamines employed for photodynamic therapy can be tested in a metabolic assay (col. 26, lines 20-50).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employed the HBr salts of any of the rhodamine derivatives disclosed Gaboury et al. (US 5,556,992), Gaboury et al. (US 5,773,460), Pal (1996), or Villeneuve (1999). The ordinary artisan would have been motivated to exchange the halogens because the HBr salts are more toxic to cells than the HCl derivatives. The ordinary artisan would have recognized that HBr rhodamine salts would have greater toxicity than their HCl counterparts. This toxicity would enhance the cell-killing ability of the rhodamine derivative, which is desirable for the purpose of killing cancer cells. The ordinary artisan would have had a reasonable expectation that the HBr salts of the compounds disclosed by Gaboury et al. (US 5,556,992 or US 5,773,460), Pal (1996), or Villeneuve (1999) would be effective to kill cancer cells because Lucas et al. teach that HBr salts are toxic to cells.

Therefore, the HBr salts of claim 1 would have been obvious over Gaboury et al. (US 5,556,992 or US 5,773,460), Pal (1996), or Villeneuve (1999) in view of Lucas et al. (US 5,871,946).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEAN C. WITZ
PRIMARY EXAMINER